This letter is being sent for your [illegible] and in the thought that you may [illegible] it. With greetings, H. J. Muller

Many thanks for sending me the index of citations — it's an extremely useful sort of thing. As for my proposal of Pincus, I realize of course that Benzer & Hershey should get a Nobel Prize, and will back them, but that will surely come, and it is longer overdue for Pincus & requires more effort because of the prejudice against this kind of achievement.

Your article was much to the point, in my opinion, in its positive aspects (see, for instance, Bernal's "The World, the Flesh, and the Devil") but I don't agree with the negative point, i.e. your case against positive eugenics, as I'll write you more legibly when I'm less busy.

As ever, Joe

x PINCUS

JAN 28 1963

Department of Zoology
204 Jordan Hall
Indiana University
Bloomington, Indiana
January 25, 1963

The Nobel Committee for Physiology or Medicine
Attention Sten Friberg, Chairman
The Royal Caroline Medical Institute
Stockholm, Sweden

Dear Sirs:

The purpose of this letter is to nominate for the Nobel Prize for Physiology or Medicine in 1963 Dr. Gregory Pincus, Research Director of the Worcester Foundation for Experimental Biology, Shrewsbury, Massachusetts. The discovery on which I would base this nomination lies in Pincus's working out, along lines original with him, of the first practicable oral contraceptive. This has been designated "enovid." Only in the past two years has the validity of this means of contraception become generally accepted in medical circles. However, since Pincus's pioneer researches on enovid first became known to specialists, several other orally taken contraceptive preparations, following the same principles of action, have been devised and offered by others. These are to be regarded as variations on the same theme and there is as yet no evidence that any of them are in an overall way superior to enovid itself.

Nevertheless, there is every reason to believe that considerable improvements in processes of manufactur of oral contraceptives, in their mode of application, in their precise chemical composition, and in the incorporation of accessory materials with them can in time be achieved. This would greatly decrease the expense and increase the suitability of oral contraception based on the principle of enovid, for use in relatively underdeveloped regions. At the present time, the use of this mode of contraception is rapidly increasing in countries having a relatively high standard of living. Thus it constitutes a major means of attack on one of the most menacing problems of our time, the population explosion.

The development and the demonstration of the efficacy of enovid represents the culmination of a lifetime. During the late 20's and early 30's Pincus, after obtaining his doctorate in Zoology at Harvard, started in on problems of mammalian genetics, reproduction, and development in general. Gradually he concentrated on the physiological and then the biochemical processes involved in ovulation, implantation and related phenomena. Beginning in the later 30's and early 40's he made pioneer contributions to the distinctive roles and properties of the steroids. It was Pincus who in the early 40's was the first to find that a steroid hormone, arising in the adrenal cortex, is able to assist the human organism under stress conditions, as in prolonged emergencies, cold, etc., a finding that was put to use by the Air Force during World War II. He also found that schizophrenics are unlike normal individuals in their production of and reaction to this steroid. (Later, after cortisone had been discovered elsewhere, it was found to be a derivative of this steroid.)

In the last twenty years Pincus and his group have made exhaustive physiological studies of the great series of related steroids, natural and artificial, to which the sex hormones also belong. In so doing the roles played by different chemical groupings was determined. The most outstanding achievement of this study has been the development of the first practical oral contraceptive. The pill developed is a combination of two substances, a progestin and an estrogen, each selected by a comprehensive sifting out process conducted on a multitude of different chemical variants.

PINCUS, G.

Large-scale tests of this medicament have been conducted for more than six years in Puerto Rico, Haiti and elsewhere, by Pincus in collaboration with John Rock, M.D. and a staff of field workers. These tests have demonstrated the long-standing reliability and safety of the method, as well as the relative insignificance of side effects. The latter are experienced by only a relatively small minority of the participants and they disappear after the first few months. At the same time, progress that is being made in the method of production of the preparation is giving hope that its cost can be greatly reduced.

Likewise important is the means for controlling menstrual function afforded by the use of this progestin-estrogen medication regime. Extreme cyclic regularity is thereby assured; the resulting cycles tend to be free of pain and are generally characterized by lightness of menstrual flow. Indeed the agents studied are now acknowledged the best available for inhibiting excessive bleeding from the uterus. Thus they are now widely used in the control of dysfunctional flow and in preparing the hemorrhagic uterus for surgical intervention. Other outcomes of the demonstrated control of uterine function have been the use of these agents in the control of endometriosis, in the alleviation of premenstrual tension, in pregnancy diagnosis, in the experimental treatment of certain uterine and cervical malignancies, and in both direct and adjuvant therapy of certain vaginal diseases. It may be added that further therapeutic potentialities of the 19-nor steroids and other progestins are still being explored, and that the establishment of their physiological effectiveness has opened wide areas for research and study.

A curriculum vitae of Gregory Pincus is also included, as well as a list, selected by myself, of some 80 of his more than 300 publications. Many important contributions have undoubtedly been omitted from this list.

Regarding Pincus's earlier work, his versatility and originality should be emphasized. His earlier work (1927-'37) included studies in genetics (mutation and inheritance in mice, diabetes inheritance in man), cytology (of different rat species), behavior (tropisms of rodents), reproductive physiology (effect of hormones on ovulation and pregnancy), and studies of mammalian eggs from stages of maturation through fertilization to implantation. Included also were studies on tissue cultures (1931), and the first successful in vitro induction and observation of ovulation, artificial activation, fertilization, and cleavage of mammalian eggs. The present writer (Muller) has investigated the major cases of mammalian parthenogenesis reported by Pincus and is convinced of their authenticity. These researches on development were gradually reduced as Pincus's findings opened up further leads into the hormonal control of ovulation and pregnancy, and into the nature and mode of action of related hormones, produced by the adrenals. This brings us to the phase of Pincus's researches, discussed at the beginning of our account, that culminated in his enovid.

In the development of this medication we have an instance where the achievement was not purely the result of "serendipity," but also of conscious seeking with a major objective in view. It represents that simultaneous seeking after truth and the achievement of major benefit to mankind which Alfred Nobel was especially desirous of fostering.

Yours sincerely,

H. J. Muller

H. J. Muller

HJM:slh
enc.